REMARKS

Status of the Claims

Claims 1-7 are pending. With entry of this amendment, claims 1-7 are currently amended, and claims 8-9 are canceled. No new matter is added; support for the amendments can be found throughout the application and claims as filed. For example, support for the pre-selected nucleic acid sequence comprising the 16s/23s or 18s/26s ribosomal RNA (rRNA) spacer region can be found on page 13, lines 10-23 of the application as filed. Other amendments have been made to clarify claim language and structure, and to correct minor typographical errors.

With entry of this amendment, claims 1-7 are currently pending and under consideration.

Claim Objections – Improper Multiple Dependent Claims

Claims 4, 6 and 7 are objected to under 37 CFR 1.75(c) as being in improper form because multiple dependent claims must refer to other claims in the alternative only (Action page 3).

Applicants note it appears that the Examiner has reviewed the claims as presented in the PCT application, and not the claims as filed with the Office. Applicants respectfully refer the Examiner's attention to the Substituted Specification as filed with the USPTO on May 10, 2005, where the claims as filed with the Office are found on pages 32-34. For reference, Applicants have attached the claims as filed, along with a photocopy of the Return Receipt Postcard acknowledging the Substituted Specification, provided herewith as Exhibit A. The claim amendments presented in this Reply reflect the claim language as filed with the Office on May 10, 2005.

Applicants assert that claims 4, 6 and 7 as filed with the Office and as presently amended are not multiple dependent claims under 37 CFR 1.75(c), and Applicants respectfully request withdrawal of the objections.

Double Patenting

The Examiner has provisionally rejected claims 1-3 and 5 on the grounds of nonstatutory obviousness-type double patenting over claims 1-3 of copending Application No. 10/534,955. Additionally, the Examiner has provisionally rejected claims 1-3 and 5 on the grounds of nonstatutory obviousness-type double patenting over claims 1-3 of copending Application No. 10/532,319.

If a "provisional" double patenting rejection in one application is the only rejection remaining in that application, the examiner should then withdraw the rejections and permit the application to issue as a patent. Application Nos. 10/534,955 and 10/532,319 are not currently allowed. Accordingly, Applicants submit if these provisional rejections are the only outstanding rejections, the present claims should be allowed. However, Applicants will consider filing Terminal Disclaimers when the present claims are indicated as otherwise allowable if/when Application Nos. 10/534,955 and 10/532,319 are allowed.

Claim Rejections – 35 U.S.C. §112

The Examiner has rejected claims 2 and 3 under 35 U.S.C. §112, second paragraph, for having insufficient antecedent basis for the limitations "a second aliquot" and "a second and a third aliquot" (Action page 5-6).

Applicants have amended claims 1-3 to correctly reference the first, second and third aliquots. Applicants assert that these amendments are fully responsive to the Examiner's assertions and respectfully request withdrawal of the §112 rejections.

Claim Rejections – 35 U.S.C. §102

The Examiner has rejected claims 1-3 under 35 U.S.C. §102(b) as being anticipated by Epsy et al. (Action page 6).

Without acquiescing to the propriety of the rejection, Applicants have amended claim 1 to recite the limitation "...specifically detecting a pre-selected nucleic acid sequence comprising the 16s/23s or 18s/26s rRNA spacer region...". The Epsy reference teaches the use of pre-selected nucleic acid sequences directed to TK and DNA Polymerase genes of HSV (Epsy Table 1 page 796); Epsy does not teach the limitation of the use of pre-selected nucleic acid sequences comprising the 16s/23s or 18s/26s rRNA spacer region. Because an asserted §102 reference must

contain all limitations of a claim to anticipate that claim, Epsy cannot be cited as anticipating claim 1. Because claims 2-3 depend from claim 1, dependent claims 2-3 cannot be anticipated by Epsy.

With entry of the amendments and for the reasons provided above, Applicants respectfully request the reconsideration and withdrawal of the §102(b) rejection of claims 1-3.

The Examiner has rejected claims 1-3 under 35 U.S.C. §102(a) as being anticipated by Larson et al. (Action page 8).

Without acquiescing to the propriety of the rejection, as discussed above Applicants have amended claim 1 to recite the limitation "...specifically detecting a pre-selected nucleic acid sequence comprising the 16s/23s or 18s/26s rRNA spacer region...". The Larson reference teaches the use of pre-selected nucleic acid sequences directed to the MSG gene family of *P. carinii* (Larson page 491, left column paragraph 7); Larson does not teach the limitation of the use of pre-selected nucleic acid sequences comprising the 16s/23s or 18s/26s rRNA spacer region. Because an asserted §102 reference must contain all limitations of a claim to anticipate that claim, Larson cannot be cited as anticipating claim 1. Because claims 2-3 depend from claim 1, dependent claims 2-3 cannot be anticipated by Larson.

With entry of the amendments and for the reasons provided above, Applicants respectfully request the reconsideration and withdrawal of the §102(a) rejection of claims 1-3.

Claim Rejections – 35 USC §103

The Examiner has rejected claims 1-3 and 5 under 35 USC 103(a) as being unpatentable over Greisen et al. in view of de Silva et al. (Action page 10). The Examiner asserts, in part, that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have extended the methods taught by Greisen to incorporate the method of determining and monitoring the temperature dependence of hybridization as taught by de Silva to arrive at the claimed invention with a reasonable expectation for success (Action pages 12-13).

Applicants respectfully assert that the Examiner has not established a proper *prima facie* case of obviousness because the cited references do not teach or suggest all of the elements as presently claimed. The Greisen reference teaches the use of pre-selected nucleic acid sequences directed to the 16s rRNA gene (Greisen abstract); Greisen does not teach the limitation in presently

amended claim 1 of the use of pre-selected nucleic acid sequences comprising the 16s/23s or 18s/26s rRNA spacer region. The de Silva reference teaches methods for determining and monitoring the temperature dependence of hybridization; de Silva does not teach the amplification and detection of either the 16s/23s or 18s/26s rRNA spacer regions.

The Examiner has not established a proper *prima facie* case of obviousness because the cited references do not teach or suggest all of the elements as presently claimed. The combination of the Greisen reference and the de Silva reference does not teach or suggest amplification and detection of either the 16s/23s or 18s/26s rRNA spacer region. Because claims 2, 3 and 5 depend from claim 1, and therefore include all of the limitations of claim 1, the arguments as stated above are also applicable to claims 2, 3 and 5. Applicants respectfully assert that the combination of references cited by the Examiner fails to teach all of the claim limitations and therefore the rejection is improper. Applicants therefore respectfully request reconsideration and withdrawal of the 103(a) rejections of claims 1-3 and 5.

CONCLUSION

Applicants respectfully request entry of the provided Amendments and Remarks, and assert that the present application is in condition for allowance and request that the Office issue a timely Notice of Allowance. If the Examiner believes that a telephone conference would expedite prosecution of this application, please telephone the undersigned at 510-814-2908.

Applicants respectfully request a 2-month extension of time to respond to this non-final Office Action mailed July 3, 2007. The response date was October 3, 2007; with the granting of this request, the response time is re-set to December 3, 2007. The commissioner is hereby authorized to charge the amount of $450, the fee due under 37 CFR §1.17(a)(2) to Deposit Account No. 50-0812. Please grant any additional extensions of time that may be required to enter this amendment and charge any additional fees or credit any overpayments to Deposit Account No. 50-0812.

Please direct all future correspondences to: Customer No. 22829.

Respectfully submitted,

Date: November 29, 2007

By: _____
Rhea C. Nersesian
Reg No. 55,488

Correspondence Address
Roche Molecular Systems, Inc.
1145 Atlantic Avenue
Alameda, California 94501
Tele: 510-814-2800
Fax: 510-814-2973

Attachment:

Exhibit A – photocopy of return receipt postcard and claims as filed on May 10, 2005.

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Customer Copy
Label 11-F June 2002

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UNITED STATES POSTAL SERVICE®

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21719-US

Serial No **N/A** Date Filed: **Even date herewith** DKT NO: **21917-US**

TITLE: **Multiplex Assay Detection of Pathogenic Organisms**

Inventors: Gerd Haberhausen, Thmas Emrich, Martin Moczko, Gregor Sagner and Gudrun Schmitz-Agheguian

DATE MAILED: May 10, 2005 ☒ CERTIFICATE OF MAILING

THE U.S. PATENT & TRADEMARK OFFICE ACKNOWLEDGES RECEIPT OF:

10/534915

☒ Transmittal Letter to the US/DO/EO/US
☒ Preliminary Amendment (3 pages)
☒ PCT Publication WO 2004/053155 & Search Report
☒ IPER (International Preliminary Examination Report)
☒ Declaration of Inventorship (2 pages)
☒ Substituted Specification (Spec 31 pgs, Claims 3 pgs (9 claims), Abstract 1 pages
☒ Application Data Sheet (3 pages)
☒ Statement Under 37 CFR 1.821
☒ Sequence Listing (4 pages + diskette)
☒ Express Mailing Label EV 338301706US
☒ Return Receipt Post Card
☒ Auth. to Charge Deposit Account No. **50-0812** for $**1000.00**

JC10 Rec'd PCT/PTO 10 MAY 2005

What is Claimed

1. A method for identification of a pathogenic organism from a predetermined group of pathogens, comprising
   a) at least partially purifying nucleic acid from a clinical sample to create a clinical specimen,
   b) subjecting at least a first aliquot of said clinical specimen to at least one amplification and detection reaction in one reaction vessel comprising
      ba) an amplification step using at least a first set of amplification primers capable of amplifying a pre-selected nucleic acid sequence region from several or all members of said predetermined group of pathogens,
      bb) a detection step using a plurality of hybridization reagents, said reagents together being capable of specifically detecting a pre-selected nucleic acid sequence region from all members of said group of pathogens, said detection step bb) comprising
         bba) monitoring hybridization of each of said hybridization reagents at a pre-selected temperature, said hybridization being indicative of at least the genus of said pathogen present in the sample, and
         bbb) monitoring temperature dependence of hybridization, said temperature dependence being indicative of at least the species of said pathogen, determining whether said amplification and detection reaction is indicative for the presence of a specific member of said pre-selected group of pathogens.
2. Method according to claim 1, wherein a first and a second aliquot each are subjected to an amplification and detection reaction independently from each other in two different reaction vessels.
3. Method according to claim 2, wherein a first, a second and a third aliquot each are subjected to an amplification and detection reaction independently from each other in two different reaction vessels.
4. Method according to claim 1, wherein an additional hybridization reagent is used for the detection of an internal control.

5. Method according to claim 2, wherein gram positive pathogenic organisms are exclusively identified the other amplification and detection reaction and gram negative pathogenic organisms are exclusively identified the amount amplification and detection reaction.

6. Method according to claim 3, wherein fungal pathogens are exclusively identified in the third amplification and detection reaction.

7. Method according to claims 2, wherein each amplification step is performed with the same thermocycling profile.

8. Composition comprising at least a first set of amplification primers and at least two hybridization reagents, characterized in that

- said at least first set of amplification primer is capable of amplifying a pre-selected nucleic acid sequence region from several or all members of a predetermined group of pathogens, and
- said at least two hybridization reagents together are being capable of specifically detecting a pre-selected nucleic acid sequence region from all members of a predetermined group of pathogens, wherein
- hybridization of each of said hybridization reagents at a pre-selected temperature is indicative for at least the genus of a pathogen present in the sample, and
- the temperature dependence of said hybridization is indicative for at least the species of said pathogen.

9. Kit comprising at least a first set of amplification primers and at least two hybridization reagents, characterized in that

- said at least first set of amplification primer is capable of amplifying a pre-selected nucleic acid sequence region from several or all members of a predetermined group of pathogens, and
- said at least two hybridization reagents together are being capable of specifically detecting a pre-selected nucleic acid sequence region from all members of a predetermined group of pathogens, wherein
  - hybridization of each of said hybridization reagents at a pre-selected temperature is indicative for at least the genus of a pathogen present in the sample, and

- the temperature dependence of said hybridization is indicative for at least the species of said pathogen.